APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,828	11/24/1999	ROLF SKOLD	2964-102P	4478

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EXAMINER
SODERQUIST, ARLEN

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

		Application No. 09/381,828	Applicant(s) Skold	
Office Action Summary		Examiner Arlen Soderquist		Art Unit 1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ___3___ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 7, 2003* _____.

2a) ☐ This action is **FINAL**.   2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-10* _____ is/are pending in the application.

　　4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 4-8, and 10* _____ is/are rejected.

7) ☒ Claim(s) *3 and 9* _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

　　Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

　　If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

　　a) ☒ All b) ☐ Some* c) ☐ None of:

　　　　1. ☒ Certified copies of the priority documents have been received.

　　　　2. ☐ Certified copies of the priority documents have been received in Application No. _____.

　　　　3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

　　*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

　　a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

4) ☐ Interview Summary (PTO-413) Paper No(s). _____

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____

1.   The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in
> section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are
> such that the subject matter as a whole would have been obvious at the time the invention was made to a person
> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the
> manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459

(1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

> 1. Determining the scope and contents of the prior art.
> 2. Ascertaining the differences between the prior art and the claims at issue.
> 3. Resolving the level of ordinary skill in the pertinent art.
> 4. Considering objective evidence present in the application indicating obviousness or
>   nonobviousness.

2.   Claims 1-2, 4-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Franchini in view of Baxter and Cunha or Renoe and Bader, Laughlin (newly cited and applied),

Li, Rodriguez or Saxberg. In the paper Franchini teaches an approach to the problem of the

dependence of the dissociation constant of weak electrolytes on the temperature and on the

solvent composition in the ethane-1,2-diol-2-methoxyethanol solvent system. This empirical

approach to clarify the problem of the dependence of the dissociation constants of weak

electrolytes on temperature and composition of mixed solvents systems (X) is applied to the

dissociation constant of picric acid in ethane-1,2-diol, in 2-methoxyethanol and in their binary

mixtures. The data are those of previous work (recalculated by means of the more accurate

Fuoss-Hsia equation) integrated by the experimental data relative to 3 new mixtures. Two

equations of the dependence of K on T and of K on X, respectively, were suggested and good

accordance between experimental and calculated values are shown. Starting from the 2

above-mentioned equations, general empirical equations for the surface $K(T,x)$ are proposed; the

average difference between calculated and experimental K values is ~8%. A three-dimensional

plot of the function $K = K(T,X$, figure 3) is presented. In the procedure section of page 1698,

Franchini teaches that the solutions of picric acid of different concentrations were made by

successive dilution of stock solutions. Franchini does not teach automated control of the dilutions in a single container.

In the abstract Baxter evaluates a simplified generalized standard additions method for calibration in the direct analysis of solid samples by graphite furnace atomic spectrometric techniques. In combining the principles of experimental design and the simplified approach to the generalized standard additions method, a useful calibration strategy was obtained for the single-component analysis of solid samples. By varying both the solid sample mass and the amount of analyte added, the observed response is defined by these 2 variables and may be geometrically described as a surface in 3-dimensional space. The use of multiple regression techniques then allows the analyte concentration in the solid to be computed from the response plane. Simultaneous blank correction and quantification was also performed. The importance of a well designed experimental lay-out and the effects of random errors or noise on the accuracy of the procedure were investigated, and some analytical results are given in the paper. The approximation of the analyte concentration obtained is fairly insensitive to curvature in the calibration function, but tends to be biased high in the presence of intense noise. This latter is a major limitation given the inhomogeneity of most solid samples which leads to irreproducible or noisy results.

In the paper Cunha discusses automated gravimetric management of solutions with a high-performance microcomputer-controlled gravimetric buret. A versatile gravimetric buret and the necessary interface that allows it to be controlled by an IBM-PC microcomputer are described. The buret employs an electronic balance that holds three 30 mL flasks. The flasks are used for delivering different titrants or standard solutions and are connected to the sensor through the bottom of the balance. The addition of the solution is controlled by poly(tetrafluoroethylene) electromechanical valves housed inside the unit. The flasks can be refilled automatically from larger reservoirs placed outside the case. Solution level sensors are used to realize automatic refill when necessary. The mass delivered from the flasks is read by the computer through an RS232C interface. The buret can, when driven by the appropriate software, perform

potentiometric, biamperometric and spectrophotometric titrations, standard additions procedures and the preparation of standard solutions.

In the paper Renoe presents an automated computer-controlled solution handling system utilizing weights. An automated sample and reagent solution preparation system, which is generally applicable in the analytical laboratory, was designed and tested. The new system utilizes an electronic sensor to weigh accurately the nominal aliquots of sample and reagent solutions that are added to a disposable beaker. Each plastic beaker on a turntable is automatically positioned on the weight sensor. Reagent and sample solutions are added by gravity feed for selected time intervals to provide nominal amounts. Each reagent or sample is accurately weighed after addition, and the beaker is then automatically moved to a stirring station while another beaker is moved into position for weight measurements. The amounts of reagents added to the beaker can be incrementally adjusted as desired. The operational modes are specified by interaction through FORTRAN programming and FORTRAN callable subroutines, which control or accumulate data concerning the system turntable, weight sensor, solution delivery devices and mixer, and the computer peripherals. The analytical utility of the system is demonstrated by data obtained in automated preparation of working curves and standard-addition procedures.

In the paper Bader presents a systematic approach to standard addition methods in instrumental analysis. Standard addition procedures in instrumental analysis are described, and variations possible with linear and nonlinear instruments are listed. Variations for linear instruments include continuous variation of standard at constant total volume, of unknown at constant total volume, of both unknown and standard at constant total volume, variable volume single addition of standard, and variable total volume with continuous variation of standard. An example of a nonlinear response and examples of radiochemical techniques are also presented. In the first paragraph Bader teaches that the standard additions methods overcome or eliminate problems due to the calibration being performed with different sample matrices and differences in instrumental response. Relative to the instant claims case 5 (page 704) is important in that a single sample has multiple additions of a standard solution of the analyte. This case teaches that

this method is particularly applicable to polarographic methods by reducing disturbances to the system and reducing the time for analysis due to changing of samples. Case 6 shows how case 5 can be applied to non-linear experiments.

In the paper Laughlin presents an expedient technique for determining solubility phase boundaries in surfactant-water systems. A stepwise dilution method is described for determining solubiity limits in surfactant-H_2O systems. Only 1 g of sample and 1 day are required to obtain reliable results. Special problems such as foaming and viscous liquid crystal phases can be dealt with. However, inner transitions involving liquid crystals are beyond the scope of the method. Samples are viewed between crossed polarizers to determine phase transition temperatures on cooling. Aliquots of H_2O are added to the original sample and measurements are repeated. In the first paragraph of the paper Laughlin teaches that prior techniques for measuring these phase boundaries require a lot of sample and effort which is not practical with small valuable research samples. These prior methods follow one of two principles of which they modified the synthetic method to arrive at the above stepwise dilution method. The procedure is found in the paragraph bridging the columns of page 239. Figure 2 shows a phase diagram determined by the technique.

In the paper Li presents a computer approach to ion-selective electrode potentiometry by two standard additions and subtractions methods through ionic strength calibration. The effect of ionic strength in standard additions and subtractions methods has been utilized for determining an unknown concentration using an ion-selective electrode without prior calibration of the electrode. In the simplest instance, only 2 standard additions or subtractions are required. An initial value of unknown concentration or electrode slope is first assumed to solve the equations repeatedly. This method gives greater accuracy than the methods which are used at present. The method was used to evaluate the unknown concentration and electrode slope. The blank solution has the same ionic strength as the standard solution in the 2 standard additions method. In the 2 standard subtractions method, a suitable blank solution is chosen. The effectiveness of computer iterative solution of the 2 standard additions method is demonstrated on a lead sample.

In the paper Rodriguez discusses validation of an analytical instrumental method by standard addition. A statistical procedure to validate an analytical methodology by standard

addition methodology is described. The data set obtained in 3 calibration experiments with standard dilutions, standard additions, and portions of sample was used. The accuracy of the analytical results is checked by comparison of analyte contents in the different calibrations and from the recovery. Mathematical expressions to estimate the statistical parameters are proposed. The statistical protocol was applied to fluorometric determination of Mo with alizarin S in vegetable tissues. In the experimental section of page 472 Rodriguez discusses the procedures used for the standard calibration -- different analyte standard solutions and replicates of each solution-- and the standard addition calibration -- continuous variations of standard at constant volume. It is clear that the standard additions method does not require replicates.

In the paper Saxberg presents a generalized standard addition method. The normal standard addition method assumes that for any 1 analyte in a sample there is an analytical sensor which responds to that analyte and no other component in the sample. When the analytical sensor is not completely selective, so-called interference effects result which can be a major source of error. The generalized standard addition method (GSAM) provides a means of detecting interference effects, quantifying the magnitude of the interferences, and simultaneously determining analyte concentrations. The GSAM as presented in the paper uses multiple linear regression to analyze multicomponent samples where the response-analyte concentration relation is of some arbitrary polynomial form; for a nonlinear polynomial relation, an iterative solution is required. In the first paragraph of the paper, Saxberg teach that the standard addition method is well known to all analytical chemists along with its use to overcome sample and/or method associated interferences such as residual matrix effects. the second paragraph teaches that in the method a linear change in the response of the analyte is assumed. Thus plotting the response change for several successive additions of the analyte to a sample with an unknown analyte concentration allows the analyte concentration to be found.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the successive dilutions of Franchini with the successive additions of an analyte containing solution of known concentration according to the teachings of Bader, Li, Rodriguez or Saxberg because of the reductions of interferences due to matrix effects and the greater accuracy

through use of a standard additions method as taught by Bader, Li, Rodriguez and Saxberg. It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the successive dilutions of Franchini with the stepwise dilutions of an analyte containing solution according to the teachings of Laughlin because of the reductions time, effort and sample as taught by Laughlin. Additionally one of skill in the art would have recognized that as taught by Baxter the standard additions method is capable of being performed with two independent variables and one dependent variable with the result being plotted as a three-dimensional graph. It would have been obvious to one of ordinary skill in the art at the time the invention was made to automate the Franchini method through use of an automated liquid handling system as taught by Cunha or Renoe because of the flexibility and versatility of liquid handling as taught by Cunha and Renoe. Additionally the Courts have held that providing a mechanical or automatic means to replace manual activity which accomplishes the same result is within the skill of a routineer in the art (see *In re Venner*, 120 USPQ 192 (CCPA 1958)).

3.   Claims 3 and 9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The art of record does not teach or fairly suggest the method as claimed in which a volume of tested sample is replaced by an equal volume of liquid having the analyte at a concentration different than the tested sample to form a new sample for testing or an apparatus as claimed which has means to control the apparatus to perform the method of claim 3.

4.   Applicant's arguments filed April 7, 2003 have been fully considered but they are not persuasive. First, the newly cited and applied Laughlin reference clearly teaches replacing the prior methods with a stepwise dilution method and shows how it reduces the labor and sample requirements of prior methods. Thus Laughlin provides an expectation that using a stepwise dilution method will reduce the effort and sample needed to produce a diagram showing phase boundaries. One of skill in the art would have clearly recognized Franchini as a method requiring large amounts or effort and materials to perform and would have replaced the serial dilutions of Franchini with the stepwise dilutions of Laughlin to obtain the benefits taught by Laughlin. Relative to the combination of Franchini with Bader applicant has not properly

understood the teachings of case 5. In the case the method can be performed in one of two alternate ways: a series of solutions having an incrementally larger portion of the standard solution or a single solution to which repeated additions are made of the standard solution. The first manner forms a series of solutions similar to the Franchini reference that are used in the subsequent measurements. Relative to the addition of standard to a single sample the second to last sentence of the section teaches the time savings since the samples do not have to be changed between measurements. The same sentence also notes an advantage in the measurement technique -- the IR drop is relatively constant -- because the measurement geometry is not disturbed between measurements. From this one of ordinary skill in the art would have recognized that performing the incremental additions on the same sample presents advantages both in the time and measurement method because the sample is not changed between successive measurement. In case 5 there is a clear advantage taught for performing the incremental additions on a single sample as compared to forming a plurality of solutions for measurement as is done by Franchini. This is in clear contradiction to how applicant has characterized Bader. Applicant has argued that Bader should be read and considered in its entirety. This is correct and when one looks at the various cases presented case 5 makes a clear comparison between a method such as used by Franchini in which multiple solutions are formed and a method in which a single solution has added to it multiple increments of another solution to change the concentration between measurements of the single solution. From that comparison Bader teaches that the second method presents advantages over the first in both time and measurement method. Thus examiner's suggestion of motivation is from a consideration of Bader in its entirety.

In response to applicant's argument that the reasons examiner has cited for combining the references are different from the problem which applicant was facing, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In response to applicant's argument that the examiner's conclusion of obviousness is based upon hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction

based upon hindsight reasoning. But so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made, and does not

include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper.

See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Relative to the argument

that the references which examiner has applied are measuring a concentration examiner points

out that pH is a representation of the acid concentration in the solution. Additionally Franchini

starts with a known concentration of a molecule that dissociates in the solution and then

determines a property of the solution (the conductance) as a measure of the dissociation that has

occurred.

5.   The prior art made of record and not relied upon is considered pertinent to applicant's

disclosure. The cited art relates to automated liquid handling and methods involving

determination of phase boundaries.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (703) 308-3989. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

For communication by fax to the organization where this application or proceeding is assigned, (703) 305-7719 may be used for official, unofficial or draft papers. When using this number a call to alert the examiner would be appreciated. Numbers for faxing official papers are 703-872-9310 (before finals), 703-872-9311 (after-final), 703-305-7718, 703-305-5408 and 703-305-5433. The above fax numbers will generally allow the papers to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

June 13, 2003

ARLEN SODERQUIST
PRIMARY EXAMINER